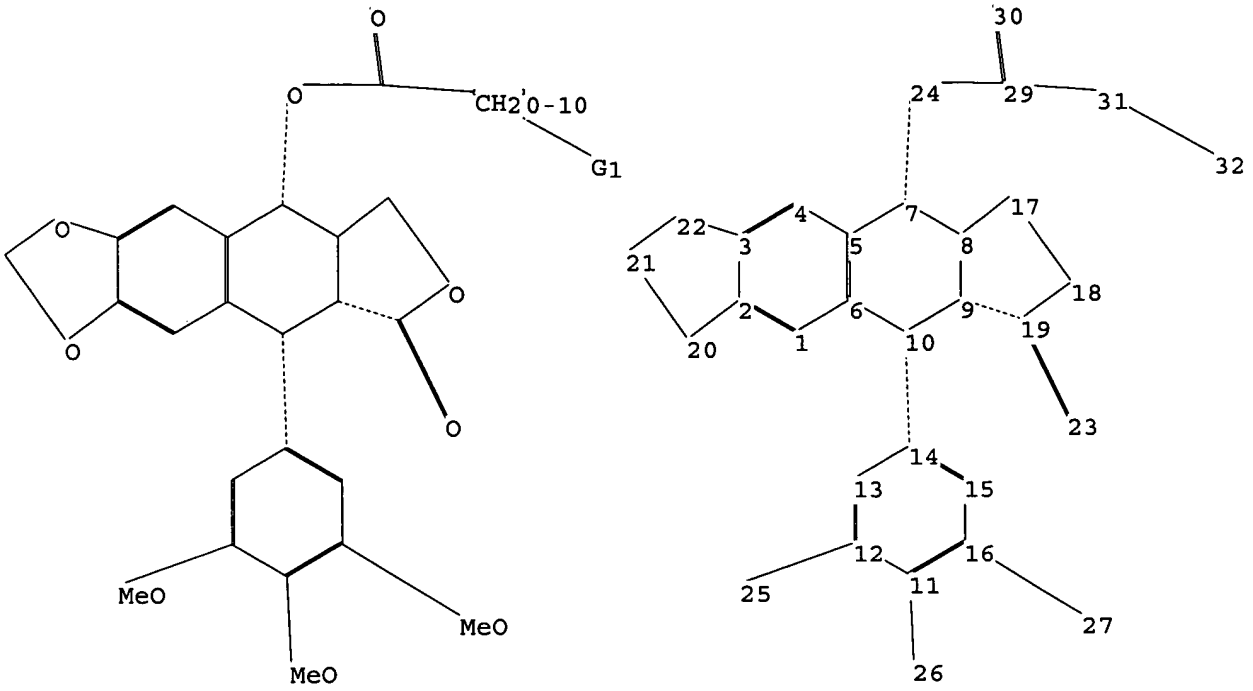

chain nodes :
23 24 25 26 27 29 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
7-24 10-14 11-26 12-25 16-27 19-23 24-29 29-30 29-31 31-32
ring bonds :
1-2 1-6 2-3 2-20 3-4 3-22 4-5 5-6 5-7 6-10 7-8 8-9 8-17 9-10 9-19
11-12 11-16 12-13 13-14 14-15 15-16 17-18 18-19 20-21 21-22
exact/norm bonds :
7-24 9-19 10-14 19-23 24-29 29-30 31-32
exact bonds :
2-20 3-22 5-7 6-10 7-8 8-9 8-17 9-10 11-26 12-25 16-27 17-18 18-19
20-21 21-22 29-31
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16
isolated ring systems :
containing 1 : 11 :

G1:O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
29:CLASS 30:CLASS 31:CLASS 32:CLASS

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L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1 ful
FULL SEARCH INITIATED 16:26:38 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    786 TO ITERATE

100.0% PROCESSED     786 ITERATIONS                              30 ANSWERS
SEARCH TIME: 00.00.01

L2           30 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   155.42     155.63

FILE 'CAPLUS' ENTERED AT 16:26:41 ON 02 AUG 2004
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FILE COVERS 1907 - 2 Aug 2004  VOL 141 ISS 6
FILE LAST UPDATED: 1 Aug 2004  (20040801/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l2
L3           15 L2

=> d ibib abs hitstr tot
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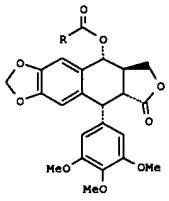
L3 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:779090 CAPLUS
DOCUMENT NUMBER: 139:292103
TITLE: Preparation of new podophyllotoxin derivatives and their therapeutic application
INVENTOR(S): Potier, Pierre; Kerkar, Brahim
PATENT ASSIGNEE(S): Fr.
SOURCE: Fr. Demande, 40 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2837824	A1	20031003	FR 2002-3903	20020328
WO 2003082875	A2	20031009	WO 2003-FR983	20030328
WO 2003082875	A3	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: FR 2002-3903 A 20020328

OTHER SOURCE(S): CASREACT 139:292103; MARPAT 139:292103
GI

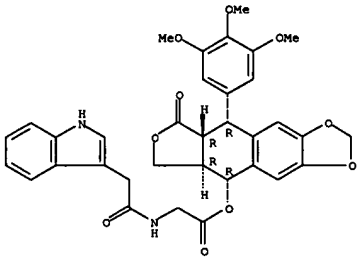


I

AB The invention relates to podophyllotoxin derivs. I (R = CH2NHC(:O)R2,

L3 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CH(OH)CHR17NHC(:O)R3, CH(OH)CHPhNHC(:O)R3, pyrrolyl-, pyridyl-, imidazolyl-, pyrazinylalkylene or -vinyl, N-oxopyridyl, quinolinyl, oxodihydroquinolinyl, etc.; R2 = (un)substituted pyrrole , imidazole, pyridine, pyrazine, indole, Ph, naphthalene, quinoline or thiazole groups;
R3 = O-(C1-4-alkyl), (un)substituted Ph (substituted with halogen or OMe);
R17 = pyridyl, C1-4-alkyl, (un)substituted Ph (substituted with halogen, NO2, OH or OMe)], their bases or addn. salts with pharmaceutically acceptable acids, in the form of enantiomers, diastereoisomers, or their mixts. (including racemic mixts.). The method of prepn. and its therapeutic application, particularly against cancer, is described. Thus,
I (R = 2-pyridyl) was prepd. from podophyllotoxin via reaction with pyridine-2-carboxylic acid in CH2Cl2 contg. DMAP and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride. The cytotoxicity of I (@ 10-100 nM) vs. human tumor cell lines (A549, HT-29, KB, KB-VMH, KB-VP2, MDA-MB-231, SK-N-SH) was tested (no data).
IT **608524-40-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of new podophyllotoxin derivs. as antitumor therapeutics)
RN 608524-40-9 CAPLUS
CN Glycine, N-(1H-indol-3-ylacetyl)-, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:372786 CAPLUS
DOCUMENT NUMBER: 138:337884
TITLE: 3α-Bromoepipodophyllotoxin-4-substituted derivative preparation and their anticancer activities
INVENTOR(S): Ma, Weiyong; He, Yong; Zhang, Chunnian
PATENT ASSIGNEE(S): Shanghai Inst. of Medical Industry, State Medicine Management Bureau, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 19 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1338457	A	20020306	CN 2000-119628	20000818

PRIORITY APPLN. INFO.: CN 2000-119628 20000818

OTHER SOURCE(S): CASREACT 138:337884; MARPAT 138:337884
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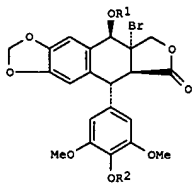
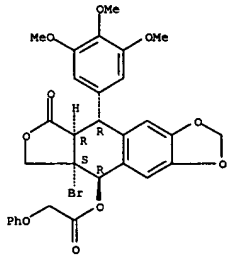


I

AB Title compds. I (R1 = H, alkyl, ester group, or substituted alkyl; R2 = H or methyl) were synthesized from epipodophyllotoxins via dehydration, obtained 3α,4-anhydro-epipodophyllotoxin, dalton reaction with N-bromosuccinimide or selective hydrolysis with hydrogen bromide, giving I
(R1 = H), further etherification with alc. or esterification with carboxylic acid in the presence of trifluoroborane di-Et etherate as catalyst. Title compds. have higher inhibitory effects on the growth of L1,210 and KB cells than VP-16.
IT **516514-96-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(3α-bromoepipodophyllotoxin-4-substituted derivs. prepn)
RN 516514-96-8 CAPLUS
CN Acetic acid, phenoxy-, (5R,5aS,8aR,9R)-5a-bromo-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L3 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L3 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:351544 CAPLUS
DOCUMENT NUMBER: 133:9081
TITLE: Modified and truncated penetratin derivatives as membrane translocation carriers for drug transport
INVENTOR(S): Fischer, M. Peter; Zhelev, Nikolai
PATENT ASSIGNEE(S): Cyclacel Limited, UK
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029427	A2	20000525	WO 1999-GB3750	19991111
WO 2000029427	A3	20001005		
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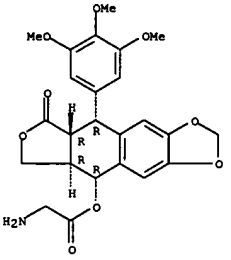
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2346616	A1	20000816	GB 1999-26719	19991111
GB 2346616	B2	20040421		
EP 1135410	A2	20010926	EP 1999-954212	19991111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002530059	T2	20020917	JP 2000-582414	19991111
AU 766489	B2	20031016	AU 2000-10630	19991111
US 2002098236	A1	20020725	US 2001-854204	20010511
PRIORITY APPLN. INFO.:			GB 1998-25000 A	19981113
			GB 1998-25001 A	19981113
			GB 1999-2522 A	19990204
			GB 1999-2525 A	19990204
			GB 1999-14578 A	19990622
			WO 1999-GB3750 W	19991111
			US 1999-438460 A3	19991112

AB The invention relates to modified and truncated forms of the membrane transport vector penetratin, a peptide comprising residues 45-58 of the Antennapedia homeodomain protein. Such truncated forms include 7-mer peptides that may in themselves include further variation. Such smaller or truncated forms of penetratin are advantageous in that they are more acceptable to the pharmaceutical industry as delivery carrier moieties, by virtue of the carrier-cargo conjugate having an advantageous immunogenicity, soly., and clearance, and in some cases advantageous efficacy as compared to using a conjugate comprised of full length penetratin. Carrier moieties are synthetically linked to a cargo moiety selected from p21WAF-derived peptides, p16-derived peptides or the drugs roscovitine, taxol, or a podophyllotoxin. The truncated penetratin-podophyllotoxin conjugate, for example, is more effective in terms of anti-proliferative activity on tumor cells while exhibiting lower generalized toxicity.

IT **251564-99-5P 254894-49-0P 254894-50-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(modified and truncated penetratin derivs. as membrane translocation carriers for drug transport)

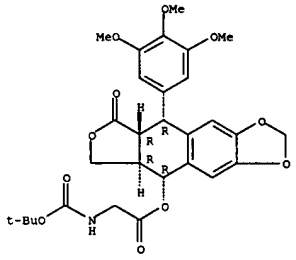
RN 251564-99-5 CAPLUS
CN Glycine, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



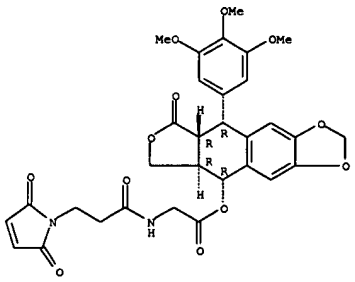
RN 254894-49-0 CAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 254894-50-3 CAPLUS
CN Glycine, N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

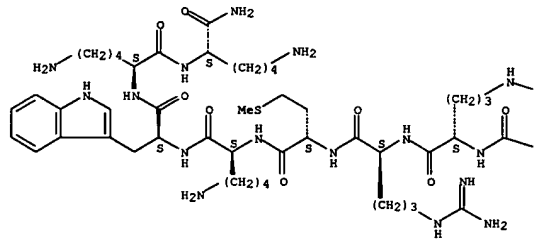


IT **254894-44-5P 254894-51-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modified and truncated penetratin derivs. as membrane translocation carriers for drug transport)

RN 254894-44-5 CAPLUS
CN L-Lysinamide, S-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]-L-cysteinyl-β-alanyl-L-arginyl-L-arginyl-L-methionyl-L-lysyl-L-tryptophyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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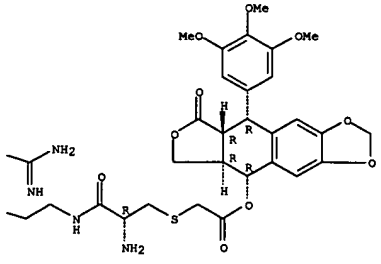
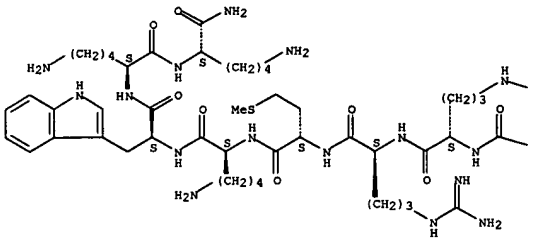


RN 254894-51-4 CAPLUS
CN L-Lysinamide, S-[1-[3-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-

L3 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]-L-cysteinyl-β-alanyl-L-arginyl-L-arginyl-L-methionyl-L-lysyl-L-tryptophyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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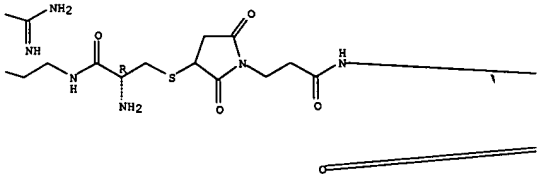

L3 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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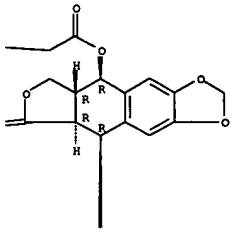

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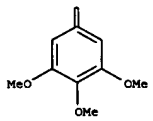


L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:34769 CAPLUS
DOCUMENT NUMBER: 132:93654
TITLE: Preparation of peptide derivatives for improved delivery of drug therapeutic agents
INVENTOR(S): Fischer, Peter Martin; Wang, Shudong
PATENT ASSIGNEE(S): Cyclacel Limited, UK
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001417	A1	20000113	WO 1999-GB1957	19990622
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2333145	AA	20000113	CA 1999-2333145	19990622
AU 9945198	A1	20000124	AU 1999-45198	19990622
AU 756014	B2	20030102		
GB 2340121	A1	20000216	GB 1999-14577	19990622
GB 2340121	B2	20000906		
EP 1093383	A1	20010425	EP 1999-928071	19990622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002519392	T2	20020702	JP 2000-557863	19990622
US 6472507	B1	20021029	US 1999-346847	19990702
US 2003119735	A1	20030626	US 2002-210660	20020731

PRIORITY APPLN. INFO.:
GB 1998-14527 A 19980703
WO 1999-GB1957 W 19990622
US 1999-346847 A1 19990702

AB The present invention relates to a novel drug delivery system for use in the improved delivery of drug therapeutic agents into target cells. The system comprises a drug moiety linked to a carrier moiety wherein the carrier moiety comprises a homeobox peptide or its fragment or derivative Thus, {[4-[N-(2,4-diamino-6-pteridinylmethyl)-N-methylamino]benzoyl]-Glu-Gly-β-Ala]4-Lys2-Lys-β-Ala-Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-Met-Lys-Trp-Lys-Lys-OH was prepared by the solid-phase method and assayed for in vitro cytotoxicity.

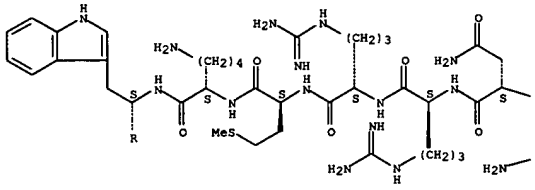
IT **254894-43-4P 254894-44-5P 254894-51-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide derivs. for improved delivery of drug therapeutic agents)

RN 254894-43-4 CAPLUS

L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN L-Lysine, S-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]-L-cysteinyl-L-arginyl-L-glutaminyl-L-isoleucyl-L-lysyl-L-isoleucyl-L-tryptophyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-arginyl-L-arginyl-L-methionyl-L-lysyl-L-tryptophyl-L-lysyl- (9CI) (CA INDEX NAME)

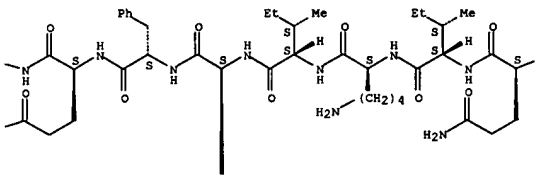
Absolute stereochemistry.

PAGE 1-A

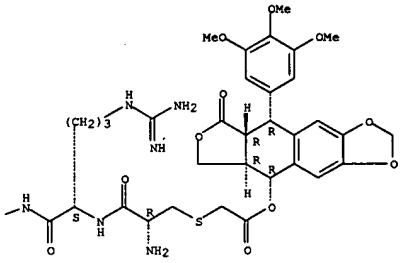


L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

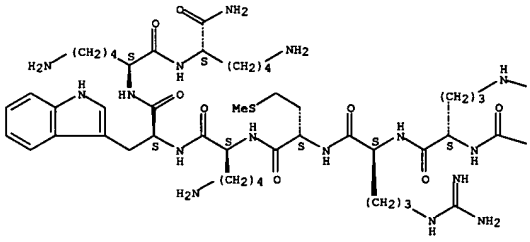


PAGE 1-C

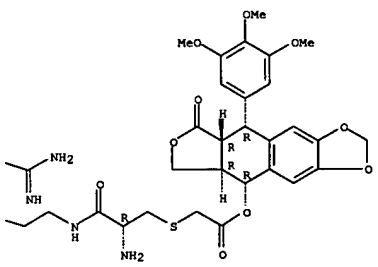


L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



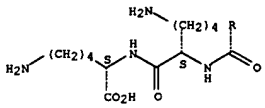
PAGE 1-B



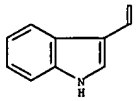
RN 254894-51-4 CAPLUS
CN L-Lysinamide,
S-[1-[3-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]-L-cysteinyl-β-alanyl-L-arginyl-L-arginyl-L-methionyl-L-lysyl-L-tryptophyl-L-lysyl- (9CI) (CA INDEX NAME)

L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



PAGE 2-B



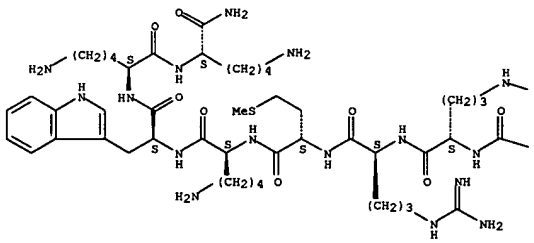
RN 254894-44-5 CAPLUS
CN L-Lysinamide, S-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]-L-cysteinyl-β-alanyl-L-arginyl-L-arginyl-L-methionyl-L-lysyl-L-tryptophyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

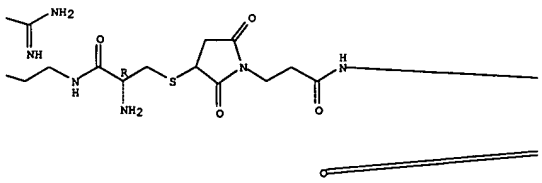
L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

PAGE 1-A

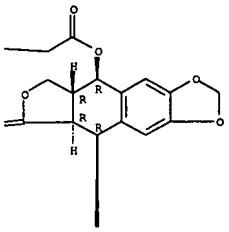


PAGE 1-B



L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-C



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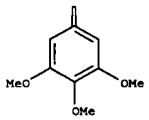
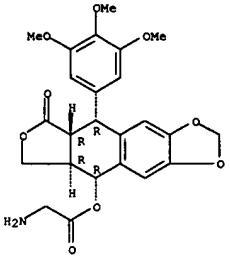


IT **251564-99-5P 254894-49-0P 254894-50-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide derivs. for improved delivery of drug therapeutic agents)
RN 251564-99-5 CAPLUS
CN Glycine, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI) (CA INDEX NAME)

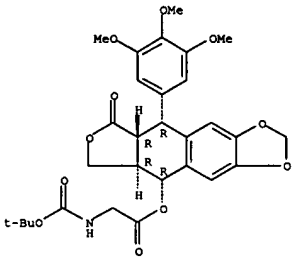
Absolute stereochemistry.

L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



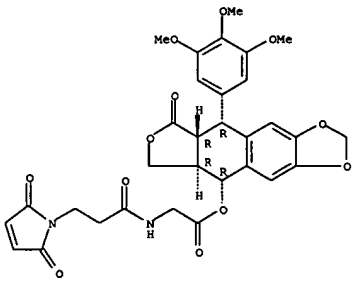
RN 254894-49-0 CAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 254894-50-3 CAPLUS
CN Glycine, N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI) (CA INDEX NAME)

L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.

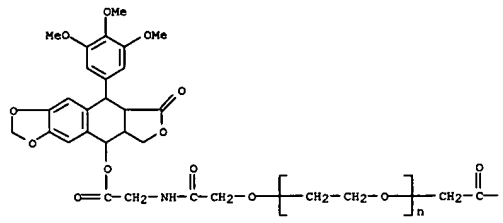


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

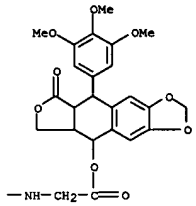
L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:568594 CAPLUS
DOCUMENT NUMBER: 132:15517
TITLE: Drug delivery of anticancer agents: water soluble 4-polyethylene glycol derivatives of the lignan, podophyllotoxin
AUTHOR(S): Greenwald, R. B.; Conover, C. D.; Pendri, A.; Choe, Y. H.; Martinez, A.; Wu, D.; Guan, S.; Yao, Z.; Shum, K. L.
CORPORATE SOURCE: Research and Development, Department of Organic and Medicinal Chemistry, Enzon, Inc., Piscataway, NJ, USA
SOURCE: Journal of Controlled Release (1999), 61(3), 281-294
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper reports on the synthesis and in vivo oncolytic activity of a series of water-soluble acyl derivs. of polyethylene glycol (PEG) conjugated podophyllotoxin. Some analogs of the polymer conjugate showed significantly better activity in a murine leukemia model than native podophyllotoxin suspended in an intralipid emulsion. Addnl., when tested i.v. against a solid lung tumor (A549) model, some conjugated analogs were equivalent to the podophyllotoxin/intralipid emulsion, while those compds. demonstrating slower rates of plasma hydrolysis (in vitro) appeared to cause greater toxicity. There appeared to be an overall correlation between the in vivo antitumor activity of the conjugate and its rate of hydrolysis in vitro, with those showing faster release possessing greater antitumor activity. In conclusion, the solubilization and predictable release of podophyllotoxin from a PEG carrier was achieved and resulted in some derivs. demonstrating, at a min., equivalency with podophyllotoxin when administered on an equal molar basis. Further studies may be warranted to assess the PEG-conjugates pharmacokinetics and therapeutic indexes in leukemic models.
IT **182064-96-6P 251565-10-3P 251565-12-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of water soluble PEG derivs. of podophyllotoxin)
RN 182064-96-6 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]amino]-2-oxoethyl]-ω-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]amino]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



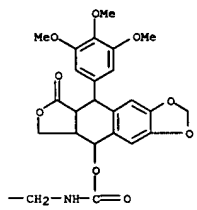
PAGE 1-B



RN 251565-10-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]carbonyl]-ω-[[[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]carbonyl]oxy]- (9CI) (CA INDEX NAME)

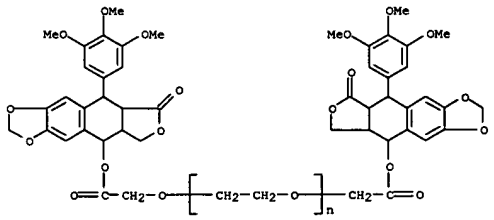
L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



IT **189160-78-9P 251564-99-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activity of water soluble PEG derivs. of podophyllotoxin)

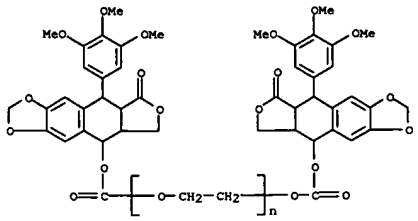
RN 189160-78-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]-ω-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)



RN 251564-99-5 CAPLUS
CN Glycine, (5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 251565-12-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]carbonyl]amino]ethyl]-ω-[2-[[[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

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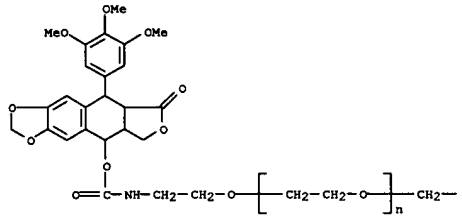
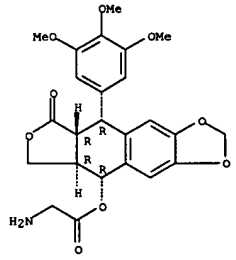


L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:175681 CAPLUS
DOCUMENT NUMBER: 130:227727
TITLE: High molecular weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,614,549.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5880131	A	19990309	US 1995-537207	19950929
US 5614549	A	19970325	US 1995-380873	19950130
CA 2208841	AA	19960808	CA 1996-2208841	19960130
WO 9623794	A1	19960808	WO 1996-US1459	19960130
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN				
AU 9649133	A1	19960821	AU 1996-49133	19960130
AU 705147	B2	19990513		
EP 807115	A1	19971119	EP 1996-905345	19960130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 10513187	T2	19981215	JP 1996-523755	19960130
NZ 302955	A	20000327	NZ 1996-302955	19960130
US 5840900	A	19981124	US 1996-700269	19960820
US 5965566	A	19991012	US 1997-914927	19970820
US 6127355	A	20001003	US 1999-277230	19990326

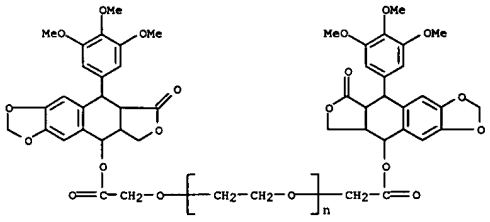
PRIORITY APPLN. INFO.:

US 1993-140346	B2 19931020
US 1995-380873	A2 19950130
US 1992-934131	B2 19920821
US 1993-28743	B2 19930309
US 1995-537207	A 19950929
WO 1996-US1459	W 19960130
US 1996-700269	A2 19960820
US 1997-914927	A1 19970820

AB High mol. weight, water-soluble prodrugs based on polyethylene glycol are described. E.g., taxol, camptothecin, and podophyllotoxin esters with PEG derivs. were prepared The prodrugs increased the life span of mice infected

L3 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

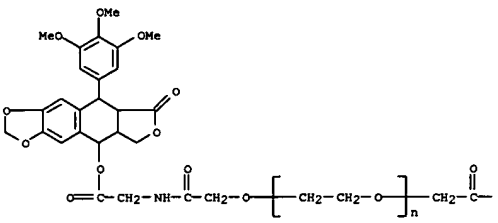
RN 189160-78-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]-ω-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)



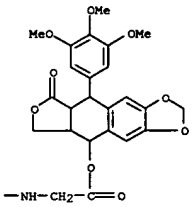
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
with murine lymphoid neoplasm compared to controls.
IT 182064-96-6P 189160-78-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(high mol. weight PEG-based prodrugs)
RN 182064-96-6 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]amino]-2-oxoethyl]-ω-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]amino]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L3 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:774306 CAPLUS
DOCUMENT NUMBER: 130:20601
TITLE: High molecular weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon Inc., USA
SOURCE: U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 537,207.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5840900	A	19981124	US 1996-700269	19960820
US 5614549	A	19970325	US 1995-380873	19950130
US 5880131	A	19990309	US 1995-537207	19950929
WO 9807713	A1	19980226	WO 1997-US14692	19970820
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9740794	A1	19980306	AU 1997-40794	19970820
AU 730244	B2	20010301		
EP 923566	A1	19990623	EP 1997-938484	19970820
EP 923566	B1	20031029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5965566	A	19991012	US 1997-914927	19970820
NZ 334283	A	20000327	NZ 1997-334283	19970820
JP 2000517304	T2	20001226	JP 1998-510949	19970820
AT 253060	E	20031115	AT 1997-938484	19970820
PT 923566	T	20040331	PT 1997-938484	19970820
US 6127355	A	20001003	US 1999-277230	19990326

PRIORITY APPLN. INFO.:

US 1993-140346	B2 19931020
US 1995-380873	A2 19950130
US 1995-537207	A2 19950929
US 1992-934131	B2 19920821
US 1993-28743	B2 19930309
US 1996-700269	A 19960820
US 1997-914927	A1 19970820
WO 1997-US14692	W 19970820

AB The present invention concerns polymeric prodrugs, DY'C(:Y)(CH2)nR1XR2, (where D is a biol. active moiety; X is an electron withdrawing group; Y and Y' are independently O or S; R1 = H, C1-6 alkyl, aryl, substituted aryl, aralkyl, heteroalkyl, n = 1-12; and R2 is a polyalkylene oxide). In

L3 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

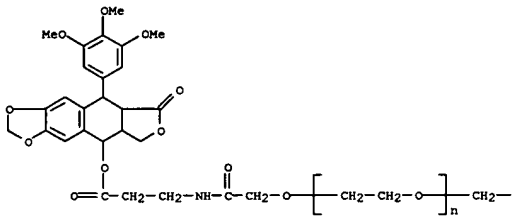
preferred embodiments, the prodrugs contain a polyethylene glycol having a
mol. wt. of at least about 20,000. Thus, camptothecin 20-O ester of
benzyloxyacetic acid was prepd.and hydrogenolyzed, and the resulting
product was treated with N,N-carbonyldiimidazole and PEG diisocyanate.
The antileukemia activity of some of the prodrugs was demonstrated.

IT **204133-48-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of high mol. weight polymer-based prodrugs)

RN 204133-48-2 CAPLUS

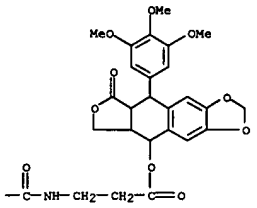
CN Poly(oxy-1,2-ethanediyl), α-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-3-oxopropyl]amino]-2-oxoethyl]-ω-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-3-oxopropyl]amino]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



L3 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

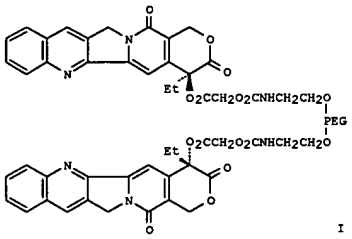
ACCESSION NUMBER: 1998:147321 CAPLUS
DOCUMENT NUMBER: 128:217533
TITLE: Preparation of high molecular weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna; Zhao, Hong
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807713	A1	19980226	WO 1997-US14692	19970820
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5840900	A	19981124	US 1996-700269	19960820
AU 9740794	A1	19980306	AU 1997-40794	19970820
AU 730244	B2	20010301		
EP 923566	A1	19990623	EP 1997-938484	19970820
EP 923566	B1	20031029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 334283	A	20000327	NZ 1997-334283	19970820
JP 2000517304	T2	20001226	JP 1998-510949	19970820
AT 253060	E	20031115	AT 1997-938484	19970820

PRIORITY APPLN. INFO.: US 1996-700269 A 19960820
US 1993-140346 B2 19931020
US 1995-380873 A2 19950130
US 1995-537207 A2 19950929
WO 1997-US14692 W 19970820

GI

L3 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

AB The present invention is directed to compns. DY'C(:Y)(CR1R2)nXR3 [D = biol. active moiety, e.g. (20S)-camptothecin, paclitaxel, podopyllotoxin, floxuridine, acyclovir, cyclosporin A; X = electron withdrawing group; Y, Y' = O, S; n = 0 - 12; R1, R2 = H, alkyl, (un)substituted aryl, aralkyl, (un)substituted heteroalkyls; R3 = non-antigenic polymer, e.g. polyethylene glycol (PEG) having a mol. weight of at least about 20,000, straight or branched (un)substituted alkyl, (un)substituted cycloalkyl, carboxyalkyl, carboalkoxy alkyl, dialkylaminoalkyl, phenylalkyl, phenylaryl; R4, R5 = H, (un)substituted alkyl, (un)substituted aryl, aralkyl, (un)substituted heteroalkyl; R4R5 = cyclic C5-C7 ring; except that R1 and R2 are both not H when n is 1 and when R3 is a substantially non-antigenic polymer]. Polyethylene glycol bound camptothecin derivative I [PEG = polyethylene glycol, 40,000 daltons (40kDa)] was prepared from (20S)-camptothecin via acylation with PhCH2OCH2CO2H in CH2Cl2 containing DIPC and DMAP, hydrogenolysis in EtOH containing cyclohexene and 10% Pd/C and condensation with PEG(40kDa) bis(2-isocyanatoethyl) ether in PhMe containing dibutyltin dilaurate. I showed antileukemic (IC50 = 7 nM vs. P-388) and antitumor activity (IC50 = 30 nM vs. human colon carcinoma HT-29).

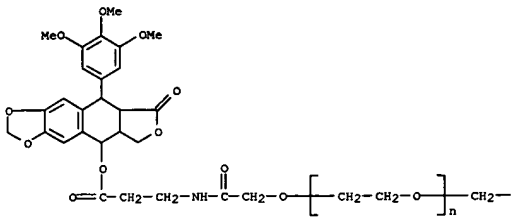
IT **204133-48-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of high mol. weight polymer-based prodrugs from natural products)

RN 204133-48-2 CAPLUS

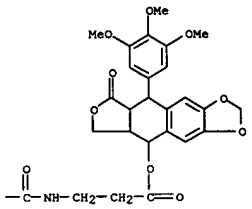
CN Poly(oxy-1,2-ethanediyl), α-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-3-oxopropyl]amino]-2-oxoethyl]-ω-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-3-oxopropyl]amino]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

L3 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

dicarboxylic acid bis(taxol-2'-diester) was prepd. and injected to P388/0 murine lymphoid neoplasm-infected mice to det. the ability of the prodrug to increase the life span of the mice.

IT **189160-78-9P**

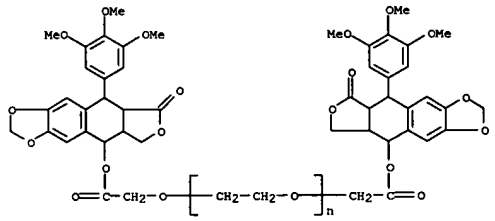
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of high-mol.-weight polymer-based water-soluble prodrugs)

RN 189160-78-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]-ω-[2-[[(5R,5aR,8aR,9R)-

5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)



L3 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:231372 CAPLUS
DOCUMENT NUMBER: 126:308799
TITLE: High-molecular-weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: U.S., 11 pp., Cont. of U.S. Ser. No. 140,346, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5614549	A	19970325	US 1995-380873	19950130
US 5880131	A	19990309	US 1995-537207	19950929
CA 2208841	AA	19960808	CA 1996-2208841	19960130
WO 9623794	A1	19960808	WO 1996-US1459	19960130
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN				
AU 9649133	A1	19960821	AU 1996-49133	19960130
AU 705147	B2	19990513		
EP 807115	A1	19971119	EP 1996-905345	19960130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 10513187	T2	19981215	JP 1996-523755	19960130
NZ 302955	A	20000327	NZ 1996-302955	19960130
US 5840900	A	19981124	US 1996-700269	19960820
US 5965566	A	19991012	US 1997-914927	19970820
US 6127355	A	20001003	US 1999-277230	19990326

PRIORITY APPLN. INFO.:

US 1992-934131	B2	19920821
US 1993-28743	B2	19930309
US 1993-140346	B2	19931020
US 1995-380873	A2	19950130
US 1995-537207	A	19950929
WO 1996-US1459	W	19960130
US 1996-700269	A2	19960820
US 1997-914927	A1	19970820

OTHER SOURCE(S): MARPAT 126:308799

AB Water-soluble prodrugs comprise hydrolyzable linkages between a polymer portion and a biol. active nucleophile, preferably taxoids. PEG 40,000

L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:618740 CAPLUS
DOCUMENT NUMBER: 125:257173
TITLE: High molecular weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623794	A1	19960808	WO 1996-US1459	19960130
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN				
US 5614549	A	19970325	US 1995-380873	19950130
US 5880131	A	19990309	US 1995-537207	19950929
AU 9649133	A1	19960821	AU 1996-49133	19960130
AU 705147	B2	19990513		
EP 807115	A1	19971119	EP 1996-905345	19960130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 10513187	T2	19981215	JP 1996-523755	19960130
NZ 302955	A	20000327	NZ 1996-302955	19960130

PRIORITY APPLN. INFO.:

US 1995-380873	A	19950130
US 1995-537207	A	19950929
US 1992-934131	B2	19920821
US 1993-28743	B2	19930309
US 1993-140346	B2	19931020
WO 1996-US1459	W	19960130

OTHER SOURCE(S): MARPAT 125:257173

AB High mol. weight, water-soluble prodrugs of taxol, camptothecin, and podophyllotoxin with PEG derivs. are prepared and hydrolysis studied to obtain prodrugs. Their neoplasm inhibiting activity was also determined

IT **182064-96-6P 182065-00-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

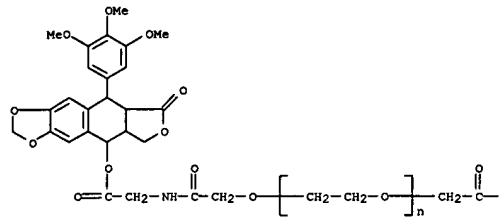
(high mol. weight polymer-based prodrugs)

RN 182064-96-6 CAPLUS

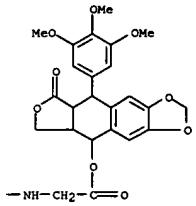
CN Poly(oxy-1,2-ethanediyl), α-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethyl]amino]-2-oxoethyl]-ω-[2-[[2-[[(5R,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-

L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
oxoethyl]amino]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

PAGE 1-A

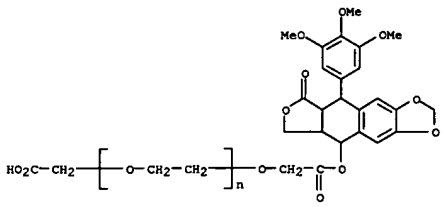


PAGE 1-B



RN 182065-00-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-[2-
[[5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]n
aphtho[2,3-d]-1,3-dioxol-5-yl]oxy]-2-oxoethoxy]-, [5R-
(5α,5aα,8aβ,9α)]- (9CI) (CA INDEX NAME)

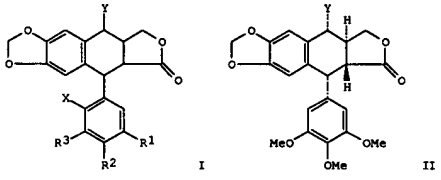
L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:7272 CAPLUS
DOCUMENT NUMBER: 112:7272
TITLE: Preparation and testing of podophyllotoxin derivatives as neoplasm inhibitors
INVENTOR(S): Nagao, Yoshuki; Tsukagoshi, Shigeru; Nakamura, Tadatake
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01117885	A2	19890510	JP 1987-275213	19871030
PRIORITY APPLN. INFO.:			JP 1987-275213	19871030

OTHER SOURCE(S): MARPAT 112:7272
GI

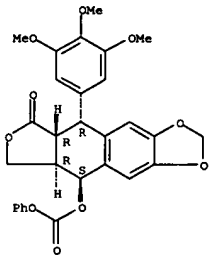


I II

AB Title compds. I [R1,R2,R3 = alkoxy; X = halo, H; Y = halo, OH, OCOR4; R4 = (hydroxyalkyl-, cyclic amino-, or benzodioxolyl-substituted) cyclic amino, (cyclic amino-substituted)alkyl amino, (≥1 OH-substituted) (un)saturated hydrocarbyl; except a combination of X = H and Y = OH] are prepared Podophyllotoxin II (Y = OH) was treated with ClCO2Ph in CH2Cl2 in the presence of pyridine to give II (Y = OCO2Ph), which was treated with 2-piperazinoethanol in CH2Cl2 to give II [Y = 4-(2-hydroxyethyl)piperazino]. II [Y = OCO(CH2)7CH:CHCH2CH:CH(CH2)4Me] at 50 mg/kg i.p. showed 157% increase in life span of mice transplanted with leukemia P-388 cells.
IT **123824-93-1P 123930-52-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of neoplasm inhibitors)
RN 123824-93-1 CAPLUS
CN Carbonic acid, 5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl phenyl

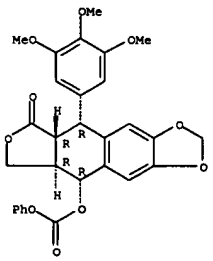
L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ester, [5S-(5α,5aβ,8aα,9β)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 123930-52-9 CAPLUS
CN Carbonic acid, 5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl phenyl ester, [5R-(5α,5aα,8aβ,9α)]- (9CI) (CA INDEX NAME)

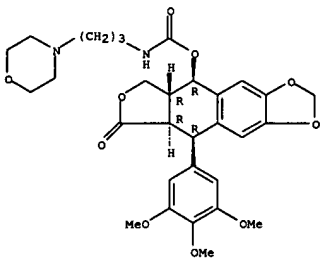
Absolute stereochemistry.



IT **123824-77-1P 123824-78-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as neoplasm inhibitor)
RN 123824-77-1 CAPLUS
CN Carbamic acid, [3-(4-morpholinyl)propyl]-, 5,5a,6,8,8a,9-hexahydro-8-oxo-9-

L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester, [5R-(5α,5aα,8aβ,9α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

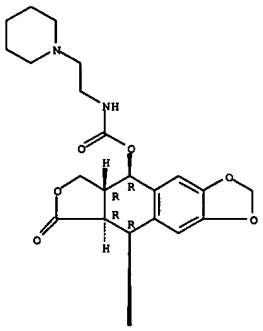


RN 123824-78-2 CAPLUS
CN Carbamic acid, [2-(1-piperidinyl)ethyl]-, 5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester, [5R-(5α,5aα,8aβ,9α)]- (9CI) (CA INDEX NAME)

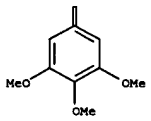
Absolute stereochemistry.

L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

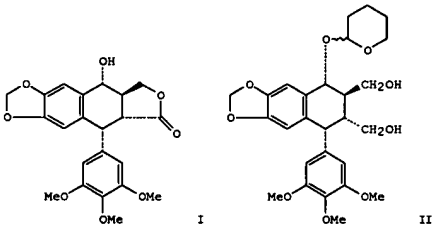


PAGE 2-A



L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1984:51350 CAPLUS
DOCUMENT NUMBER: 100:51350
TITLE: Antitumor agents. LXII: Synthesis and biological evaluation of podophyllotoxin esters and related derivatives
AUTHOR(S): Levy, Ron K.; Hall, Iris H.; Lee, Kuo Hsiung
CORPORATE SOURCE: Sch. Pharm., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: Journal of Pharmaceutical Sciences (1983), 72(10), 1158-61
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II

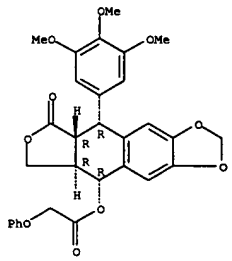
AB Synthetic esters of the C-4 hydroxyl group of podophyllotoxin (I) were prepared In addition, esters were synthesized using the diol system of tetrahydropyranylpodophyllol (II), produced by reducing the lactone ring of tetrahydropyranylpodophyllotoxin with LiAlH4. Six compds., the acrylate, 3,3-dimethylacrylate, phenoxyacetate, and Et adipate of I as well as podophyllol and tetrahydropyranyl podophyllol dimesylate, showed significant activity when tested using the P-388 lymphocytic leukemia at 3 mg/kg/day. None of the esters showed higher activity than that showed by I when tested at the same dosage level.

IT **88302-56-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of)

RN 88302-56-1 CAPLUS
CN Acetic acid, phenoxy-, 5,5a,6,8,8a,9-hexahydro-8-oxo-9-(3,4,5-trimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl ester, [5R-(5α,5aα,8aβ,9α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

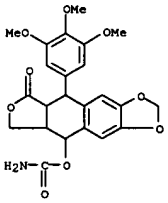


L3 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1968:504924 CAPLUS
DOCUMENT NUMBER: 69:104924
TITLE: Immunosuppressive activity of podophyllum compounds and other cytostatic agents
AUTHOR(S): Lazary, S.; Staehelin, H.
CORPORATE SOURCE: Pharm.-Toxikol. Forsch., Sandoz A.-G., Basel, Switz.
SOURCE: Int. Congr. Chemother., Proc., 5th (1967), Volume 3, 317-22. Editor(s): Spitzy, K. H. Verlag Wiener Med. Akad.: Vienna, Austria.
CODEN: 20JJA4
DOCUMENT TYPE: Conference
LANGUAGE: German

AB The immunosuppressive activity of the following agents was tested in female albino mice immunized using foreign erythrocytes: podophyllotoxin (I), carbamoylpodophyllotoxin (II), podophyllinic acid 2-ethylhydrazide (III), Proresid (IV, podophyllotoxin β-D-benzylideneglucoside), N-deacetyl-N-methylcolchicine (V), 5-fluorouracil (VI), ibenzmethyzine (VII), 6-mercaptopurine (VIII), verrucarin A (IX), diacetoxyscirpenol (X), and busulfan (XI). Suppressive indices (Nathan, et al., 1961) for various doses are given. The following L.D.17 and L.D.50 values (in mg./kg./day after 5 days of administration) were: I 2.8 and 8.0, II 29 and 42, III 85 and 118, IV 90 and 110, IX 0.71 and 1.04, X 2.4 and 4.5, VII 275 and 413, VI 22 and 40, VIII 69 and 102, V 6.9 and 13, and XI 23 and 33. Therapeutic indexes (LD17/immunosuppressive dose) ranged <1-2, except for VII (.apprx.6).

IT **13091-63-9**
RL: BIOL (Biological study)
(antibody formation inhibition by)

RN 13091-63-9 CAPLUS
CN Podophyllotoxin, carbamate (8CI) (CA INDEX NAME)



L3 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1967:464383 CAPLUS
DOCUMENT NUMBER: 67:64383
TITLE: New derivatives of podophyllotoxin
INVENTOR(S): Kuhn, Max; Von Wartburg, Albert; Renz, Jany
PATENT ASSIGNEE(S): Sandoz Ltd.
SOURCE: Fr., 4 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

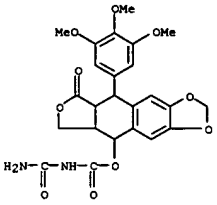
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1455540		19661014		
FR 5224			FR	
PRIORITY APPLN. INFO.:			SE	19641118

GI For diagram(s), see printed CA Issue.

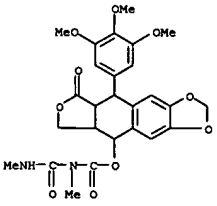
AB Podophyllotoxin allophanates (I) are prepared by treating podophyllotoxin (II) (I, one of the R1 = OH and the other is H; R2 = OMe or OH) with allophanyl chloride and alkyl isocyanate, resp. Thus, 2.8 g. allophanyl chloride was added in small portions with stirring to a solution of 3 g. II in 10 ml. C5H5N kept at 0-20° and the reaction mixture kept 4 hrs., then evaporated in vacuo. The residue was extracted with CHCl3 to give podophyllotoxin allophanate, m. 229-31°, [α]20D -127.3° (all rotatory powers in CHCl3). The podophyllotoxin α,γ-dimethylallophanate, m. 204-7°, [α]20D -155.2°, was obtained by adding 100 mg. anhydrous AcONa to a solution of 1.5 ml. methyl isocyanate in 5 ml. absolute C5H5N and the mixture kept 1 hr. at 25°. II (1 g.) was then added to this mixture, the temperature kept at 35-40° for 20 hrs., and the reaction solution was evaporated The residue was extracted with CHCl3 to give nearly equal parts of methyl carbamate and α,γ-diethylallophanate, derivs. of II. The latter derivative was eluted first with CHCl3 on silica gel and recrystd. from EtOH. However, the next fractions eluted with the same solvent contained the methylcarbamate derivative Similarly, podophyllotoxin α,γ-diethylallophanate, m. 229-31°, [α]20D -149°, was prepared from ethyl isocyanate. Also, β-peltatin allophanate, m. 190-95°, [α]20D -136°, was obtained by using β-peltatin instead of II. When HCN (from depolymn. of cyanuric acid) was used instead of allophenyl chloride in the first experiment, a mixture of podophyllotoxin carbamate and allophanate was obtained which were separated by chromatog. on silica gel. α-Peltatin, 4-demethyldeoxypodophyllotoxin, and 4-demethylpodophylotoxin can also be used instead of II. I possess specific cytostatic and antimitotic effects.

IT **15381-85-8P 15381-86-9P 15381-88-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L3 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 15381-85-8 CAPLUS
CN Allophanic acid, ester with podophyllotoxin (8CI) (CA INDEX NAME)

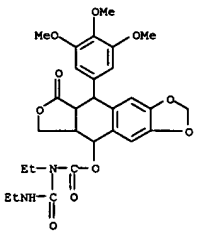


RN 15381-86-9 CAPLUS
CN Allophanic acid, 2,4-dimethyl-, ester with podophyllotoxin (8CI) (CA INDEX NAME)



RN 15381-88-1 CAPLUS
CN Allophanic acid, 2,4-diethyl-, ester with podophyllotoxin (8CI) (CA INDEX NAME)

L3 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1966:404012 CAPLUS
DOCUMENT NUMBER: 65:4012
ORIGINAL REFERENCE NO.: 65:719g-h,720a-e
TITLE: Podophyllotoxin and peltatin carbamates
PATENT ASSIGNEE(S): Sandoz Ltd.
SOURCE: 16 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

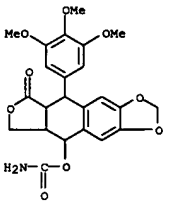
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6510414		19660214	NL	19640812

AB 4'-Dimethyldeoxypodophyllotoxin (4'-dimethylsilicicoline) (I) (250 mg.) in 2 cc. dry C5H5N heated 40 hrs. at 50° with 0.4 cc. EtNCO in a sealed vessel yielded the 4'-ethylcarbamate of I, m. 215-20° (MeOH), [α]20D-95.8° (CHCl3). I (250 mg.) in 1 cc. dry C5H5N and 0.4 cc. EtNCO heated 18 hrs. at 50° yielded the 1,4'-bis-(N-ethylcarbamate) of I, m. 203-16° (MeOH), [α]20D-116.5° (CHCl3). α-Peltatin (II) (250 mg.) gave similarly the 8,4'-bis(N-ethylcarbamate) of II, m. 219-28° (MeOH), [α]20D-174.5° (dry C5H5N). Podophyllotoxin (III) (10 g.) in 250 cc. CH2Cl2 treated with excess HOCN in a stream of CO2 and kept 20 hrs. at 20° yielded the carbamate (IV) of III, m. 196-8° (MeOH), [α]20D-144° (CHCl3). III (1 g.) in 20 cc. CH2Cl2 and 2.5 cc. dry C5H5N treated at -15° with 2 g. H2NCOCl in 10 cc. C6H6 and kept 1 hr. at -15° and 15 hrs. at 20° gave IV, m. 188-90°, [α]20D-140° (CHCl3). III (2 g.) in 5 cc. dry C5H5N treated 22 hrs. at 35-40° with 1 cc. MeNCO, and the product chromatographed on silica gel yielded the methylcarbamate of III, m. 214-16° (EtOH), [α]20D-140° (CHCl3). III (12 g.), 30 cc. dry C5H5N, and 6 cc. EtNCO heated 5 hrs. at 50° gave the ethylcarbamate of III, m. 107-11°, [α]20D-134° (CHCl3). III was converted similarly to the following derivs. (m.p., [α]20D in CHCl3, reaction time in hrs., and reaction temperature given): N-butylcarbamate, 83-7°, -126.1°, 5, 50-60°; N-phenylcarbamate, 125-8°, -115% 2, 40°; N-acetylcarbamate, 212-14°, -125°, 1, 40°; N-benzylcarbamate, 105-10° (AcOEt-pentane), -117.2°, 5, 50°. Epipodophyllotoxin with PhNCO gave similarly the N-phenylcarbamate during 2 hrs. at 40°, m. 217-20° (MeOH), [α]20D-124.5° (CHCl3). β-Peltatin (V) (250 mg.) in 1 cc. absolute C5H5N treated 20 hrs. at 50° with 0.20 cc. EtNCO yielded the amorphous N-ethylcarbamate (VI) of V, 120-4°, [α]20D-130.7° (CHCl3). Similarly were prepared the following derivs. of V (same data given): N-methylcarbamate, 140-5°, -135.5°, 22, 30-5°; N-benzylcarbamate, 109-14° (AcOEt-pentane), -117.2° (c 0.685, CHCl3). V (2.1 g.) in 50 cc. CH2Cl2 treated with cooling with 3 g. COCl2 in 30 cc. CH2Cl2 and then with 0.8 cc. C5H5N and 5 cc. CH2Cl2, kept 1 hr., and worked up gave the ClCO2 ester of V; a 1-g. portion in 15 cc. 3:1 C6H6-CH2Cl2 treated dropwise with 0.4 cc. EtNH2 in 10 cc. C6H6 yielded VI, m. 128-32°, [α]20D-131.5°

L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(CHCl3). V (1 g.) and 500 mg. Me2NPh in 15 cc. CH2Cl2 added dropwise at 0-5° to 10 cc. 10% COCl2 in CH2Cl2, kept 12 hrs. at 20°, and the crude product treated in 25 cc. CH2Cl2 at -10° with 1.25 cc. Et2NH in 25 cc. CH2Cl2 yielded the N-diethylcarbamate of V, m. 107-12°, [α]20D-133.2° (c 0.375, CHCl3). III (25 g.) and 1 cc. (CF3CO)2O and 100 cc. 4% HOCN in CH2Cl2 kept 8 hrs. at 20° yielded IV, m. 195-9°. V (2 g.) and 0.4 cc. (CF3CO)2O treated 20 hrs. at 20° with 20 cc. 3% HNCO and then again with 10 cc. 3% HNCO-CH2Cl2 and 0.2 cc. (CF3CO)2O, and worked up after 24 hrs. yielded carbamate of V, m. 146-54°, [α]20D-129.0° (c 0.537, CHCl3). NaOCN (20 g.) ground in a mortar with 30 cc. EtOH and filtered, the residue dissolved in 180 cc. H2O at 70°, and the soln. cooled to 20° and stirred dropwise into 800 cc. Me2CO pptd. activated NaOCN. III (51 g.) in 200 cc. CH2Cl2 and 5 g. dry activated NaOCN treated dropwise during 10 min. with stirring with 7 cc. (CF3CO)2O, kept 1 hr., treated again with 6.5 cc. (CF3CO)2O and 5 g. NaOCN and after 2 hrs. with 5 cc. (CF3CO)2O and 5 g. NaOCN, and stirred 15 hrs. at room temp. yielded IV, m. 193-8°. III (10 g.), 11 g. H2NCO2Et, and 500 mg. (tert-BuO)3Al [or (isoPrO)3Al] in 85 cc. dry C6H6 refluxed 3-6 hrs. while replacing 20 cc. distillate/hr. by fresh C6H6, treated with 250 mg. fresh catalyst, and heated an addnl. 9-6 hrs. yielded IV, m. 190-2° (MeOH), [α]20D-139.5° (CHCl3). I (2 g.) in 25 cc. Me2CO and 15 cc. H2O refluxed 2 hrs. with 5 cc. concd. HCl yielded 4-dimethylepipodophyllotoxin, m. 228-30° (MeOH), [α]D-69.8° (C 0.630, CHCl3).

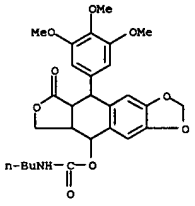
IT **13091-63-9**, Podophyllotoxin, carbamate **13091-64-0**, Podophyllotoxin, butylcarbamate **13091-65-1**, Podophyllotoxin, carbanilate **13091-66-2**, Carbamic acid, acetyl-, ester with podophyllotoxin **13264-47-6**, Carbamic acid, benzyl-, ester with podophyllotoxin **13381-44-7**, Podophyllotoxin, ethylcarbamate **14670-31-6**, Podophyllotoxin, methylcarbamate **14732-07-1**, Epipodophyllotoxin, carbanilate
(preparation of)

RN 13091-63-9 CAPLUS
CN Podophyllotoxin, carbamate (8CI) (CA INDEX NAME)

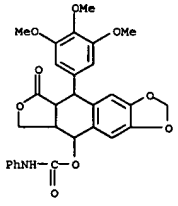


RN 13091-64-0 CAPLUS
CN Podophyllotoxin, butylcarbamate (7CI, 8CI) (CA INDEX NAME)

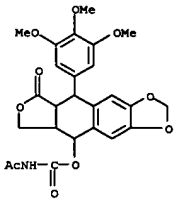
L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 13091-65-1 CAPLUS
CN Podophyllotoxin, carbanilate (7CI, 8CI) (CA INDEX NAME)

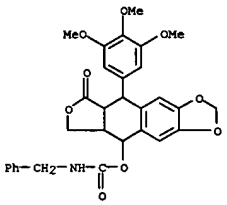


RN 13091-66-2 CAPLUS
CN Carbamic acid, acetyl-, ester with podophyllotoxin (8CI) (CA INDEX NAME)

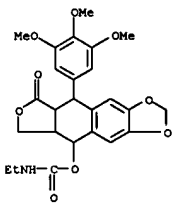


RN 13264-47-6 CAPLUS

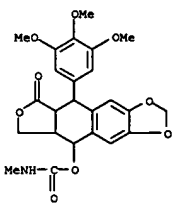
L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Podophyllotoxin, benzylcarbamate (7CI, 8CI) (CA INDEX NAME)



RN 13381-44-7 CAPLUS
CN Podophyllotoxin, ethylcarbamate (7CI, 8CI) (CA INDEX NAME)



RN 14670-31-6 CAPLUS
CN Podophyllotoxin, methylcarbamate (7CI, 8CI) (CA INDEX NAME)



L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 14732-07-1 CAPLUS
CN Epipodophyllotoxin, carbanilate (7CI, 8CI) (CA INDEX NAME)